

Appl. No. 10/614,599  
Amendment dated November 13, 2006  
Reply to Office Action of August 1, 2006

**Amendments to the Drawings:**

Enclosed herewith are annotated figure sheets and replacement figure sheets 1, 4, 5, and 8.

Attachment: Replacement Sheet

### **REMARKS**

Applicants request entry of this Amendment and reconsideration of the claims. With entry of this amendment, claims 1-18, 20-37, and 39-41 are cancelled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of these claims in one or more continuation applications.

With this Amendment, claims 19 and 38 are amended, and claims 42-75 are added. Support for the new claims can be found throughout the specification, including for example at page 66, lines 1-5; page 85, line 15 to page 91, line 9; and page 95, line 11 to page 97, line 10.

### **Priority Claim**

Amendment to the specification is requested to correct the priority claim originally made with filing of the present application on July 7, 2003 by preliminary amendment. In the priority claim made in the preliminary amendment, the filing date of provisional application USSN 60/166,177 was identified as November 17, 1999, while the correct date is November 18, 1999. A copy of the post card evidencing the correct deposit date for the provisional application is supplied. The priority claim was acknowledged on the first filing receipt, therefore the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. An Application Data Sheet with the correct priority information was previously submitted.

### **In the Drawings and Sequence Listing**

The Application as filed contained 12 sheets of figures, however only 9 sheets were intended for the application because sheets 4, 5 and 6 were submitted twice and out of order. To assist the Office in correction, replacement sheets and marked-up copies of all sheets are submitted in proper order. Specific amendments to selected Figures are also presented and noted below.

Figure 1 is amended to indicate that amino acids 15-118 of SEQ ID NO:6 are shown. Duplicate Figure 4B on Sheet 4 is deleted. Figure 4A originally presented on Sheet 5 is enlarged and represented on Sheets 4 and 5. The appearance of "SEQ ID NO:49" in Figure 7 on Sheet 8 caused the Examiner to issue an objection to the Sequence Listing in the parent case. "SEQ ID

NO:49” is a typographical error and has been corrected to “SEQ ID NO:48.” SEQ ID NO:48 properly appears in the Sequence Listing.

The sequences appearing in Figures 4B-4E are objected to as being labeled as SEQ ID NO:3, SEQ ID NO: 39, SEQ ID NO:40, or SEQ ID NO:6 but failing to correspond to those sequences in the Sequence Listing. Those figures are amended to indicate that portions of SEQ ID NO:3 and portions of SEQ ID NO:6, are represented in Figures 4B-4E. SEQ ID NO:39 in Figure 4B corresponds to residues 1-101 of SEQ ID NO:39 (shown completely in Figure 4C) and has been so labeled. SEQ ID NO:40 in Figure 4C is now SEQ ID NO: 49. A replacement Sequence Listing is being supplied including SEQ ID NO:49 in Figure 4C.

Applicant's respectfully request acceptance of the Replacement Sheets and Sequence Listing. No new matter is introduced.

#### **In the Specification**

The Examiner objected to the Brief Description of the Drawings as erroneously citing SEQ ID NO:4 in the description of Figure 3, and further objected to Figure 3 as not mentioning SEQ ID NO:38. The descriptions of the figures are amended at pages 5-6 to conform to the specification description, drawings, and sequence listing. The description for Figure 3 is amended to clarify the relationship between SEQ ID NO:38, shown in the Figure and SEQ ID NO:4. The amendment is supported in the original figure and in the specification at page 9, lines 25-27.

The description for Figures 4B and 4C and other description in the specification identified which regions of SEQ ID NO:3 and SEQ ID NO:6 are represented in Figures 4B and 4C. The sequences for SEQ ID NO:3 and SEQ ID NO:6 presented in the Sequence Listing match the sequences presented in the specification at pages 8 and 9 and match portions displayed in Figures 4B and 4C. The amino acid numbers are corrected in the description of the Figures on page 3 and also described on page 10 to correspond with the sequential residue numbering presented in the Sequence Listing. Correction does not introduce new matter.

The description for Figure 7 now identifies SEQ ID NO:48 as the complementary strand sequence of human EST AA315020 (SEQ ID NO:4). This amendment is supported by Figure 7

as originally filed, the description for human EST AA315020 at page 8, lines 14-24, and further figure description at page 88, lines 15-30.

No new matter is introduced. Entry of the above amendments is respectfully requested.

### **Claim Objections**

The Examiner objected to claim 19 as encompassing non-elected subject matter, and required an amendment to limit to the elected invention. Applicants respectfully traverse. The elected group V containing claims 19 and 38 is directed to a method of determining the presence of a nucleic acid in a sample. Claim 19 is so directed. Applicants respectfully request clarification and further believe that if claim 19 does encompass additional subject matter, that the claim should be treated as a linking claim –thereby not requiring amendment to remove unelected subject matter. Applicants request withdrawal of the objection.

### **35 U.S.C. § 101 and 35 U.S.C. § 112, ¶1 – Utility**

At page 9 of the Office Action, the Examiner rejected claim 19 under 35 U.S.C. § 101, asserting that the present invention is not supported by a credible, specific and substantial asserted utility or a well-established utility. In a related rejection at page 13, the Examiner asserts that lack of utility constitutes a failure to enable the skilled artisan to use the method of the current invention.

Applicants do not have to provide evidence sufficient to establish that an asserted utility is true beyond a reasonable doubt. *In re Irons*, 340 F.2d 974, 978 (CCPA 1965). Nor do Applicants have to provide evidence that establishes the asserted utility as a matter of statistical certainty. *Nelson v. Bowler*, 626 F.2d 853, 856-867 (CCPA 1980). Rather, Applicants only have the burden of presenting evidence that leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true. MPEP § 2107.02 (emphasis in original).

Claim 19 is directed to a method for determining the amount of a nucleic acid encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 3 or a polypeptide having at least 90% sequence identity to amino acid sequence SEQ ID NO:6, wherein enhanced expression of the nucleic acid molecule is indicative of cancer or inflammation in a cell sample.

As an initial matter, Applicants submit that the Examiner is requiring a higher standard of proof than is required by the utility standard. Applicants submit that they have described nucleic acid and amino acid sequences for both human and mouse polypeptides. Applicants have shown that these sequences are upregulated in a variety of tumor cell types. Applicants have identified that the amino acid sequences share homology to the S100 family of cytokines and further that S100 family of proteins is associated with tumor cells. Applicants submit that one of skill in the art reading the specification would understand that the nucleic acids as claimed would serve as a marker for tumors more likely than not.

The Examiner seems to be requiring that Applicants prove that the S100 polypeptide have a certain function or mechanism of action. Applicants submit that for claims directed to methods of detecting cancer or inflammation all that is required is to show that expression is upregulated in tumor cells. Applicants have shown that expression of the nucleic acid encoding a polypeptide of SEQ ID NO:6 or having at least 90% sequence identity to the sequence of SEQ ID No:6 is linked to tumors. The utility standard does not require proof of function or mechanism of action to establish utility for the claimed methods.

The Examiner asserts on pages 8-10 of the Office Action that citing the similarity of SEQ ID NO:6 to S100 cytokine is insufficient to show that the activity of the polypeptide is similar to that of S100 cytokine activity for any of the applications described in the specification. However, the sequences have strong similarity, and the skilled artisan understands that structure is related to function. Thus, the strong similarity in structure would more than likely lead a skilled artisan to conclude that the asserted utility is more likely than not true.

To confirm the role that SEQ ID NOs: 5 and 6 have in tumors, the expression of SEQ ID NO:5 was used to probe a broad array of tissues and cell lines (page 85, line 14 to page 88, line 3). Tissues that were probed included pancreas, thyroid; adrenal, salivary and pituitary glands; brain, spinal cord, heart, skeletal muscle, bone marrow, thymus, spleen, rectal, stomach, small intestine, liver, lung, mammary gland, ovary, uterus, placenta, and prostate. Cells that were probed included those derived from carcinomas, such as renal, central nervous system, colon, lung ovarian, prostate, colon, gastric and melanoma carcinomas. It was found that SEQ ID NO:5, is strongly and differentially expressed in pancreatic, liver, lung, breast, ovarian, colon, and gastric tumor cells as compared to the wild-type counterparts. The Examiner's attention is

drawn to Table 8. In contrast to the Examiner's interpretation of the data, it is clear to one of skill in the art that SEQ ID NO:5 is over-expressed and, therefore, can be used at least to detect colon, pancreas, lung, stomach, and liver cancer as presented in Table 8. Additional results were obtained in human tumor biopsies where SEQ ID NO:5 mRNA was probed for expression (page 88, line 12 to page 91, line 8). Substantial up-regulation was seen in lung, thyroid, breast, kidney, bladder, ovarian, and stomach cancers (*see* Table 9, pages 90-91).

The Examiner further asserted on page 12 that Applicant's other claimed utilities are neither specific nor substantial. Applicants assert that the evidence provided above establishes specific and substantial utility for the claimed methods. Applicants also disagree that further utilities are lacking. Applicants assert that methods of measuring levels of nucleic acids encoding SEQ ID NO:3 and 6 can be useful to test potential agents that can, for example, inhibit over-expression of SEQ ID NO:3 and/or 6 in an *in vitro* method or an animal model (page 68, lines 6-9). For example, the specification describes using animal models for atherosclerosis. See page 72, lines 22-30. Other animal models involve examining the effect of agents that inhibit over-expression of SEQ ID NO:3 in animal models of graft vs. host or autoimmune disease. See page 76, line 16 to page 77, line 1. The question is not whether the claimed method has inferior or superior utility, but rather does it have utility. The specification is sufficient such that a person of skill in the art would conclude the method of determining the amount of nucleic acids encoding a polypeptide having at least 90% identity to the amino acid sequence of SEQ ID NO:6 can be used successfully for one or more of the uses described above and, therefore, has utility.

Based on the foregoing, Applicants request withdrawal of the 35 U.S.C. § 101 rejection.

### **35 U.S.C. § 112, ¶1 Enablement**

On page 13 of the current Office Action, the Examiner rejected claim 19 as not enabling a skilled artisan to use the invention as claimed because of the alleged lack of utility. The specification is further asserted to lack enablement for SEQ ID NO:6 or nucleic acid sequences encoding variants of SEQ ID NO:3 and SEQ ID NO:6. The Examiner further asserted that there is nothing in the specification that shows what variant sequence is overexpressed in the specific tumors. At page 14, the Examiner further contended that claim 19 is non-enabling because it

encompasses an unreasonable number of inoperative polypeptides, which a skilled artisan would not know how to use. Applicants respectfully traverse.

The legal standard for enablement under 35 U.S.C. § 112 requires that “[...] a patent specification must disclose sufficient information to enable those skilled in the art to make the claimed invention.” *Hormone Research Foundation, Inc. v. Genentech*, 15 USPQ2d 1039, 1047 (Fed. Cir. 1990) (emphasis added). It is a well accepted premise that §112 ¶1 requires only that a patent specification describe to one of ordinary skill in the art how to make and use the claimed invention without undue experimentation. Under the law of enablement, a specification which teaches how to make and use the invention in terms which correspond in scope to the claims must be taken as satisfying the enablement requirement unless there is reason to doubt the objective truth of the specification. In re Marzocchi, 169 USPQ 367, 369 (CCPA 1971). It is incumbent upon the Examiner to explain why one skilled in the art would doubt the truth of statements made in the specification, and provide back up assertions with acceptable evidence or reasoning which is inconsistent with the teachings of the specification. *Id.* at 370. Absent evidence to the contrary, the specification must be assumed to be enabling.

With respect to the Examiner’s contention that the claimed methods are not enabled, Applicants respectfully disagree. Applicants have described and shown nucleic acid and amino acid sequences useful in the claimed methods. Applicants have described how to measure the level of expression of the nucleic acids in a number of different tissues. Applicants have shown upregulation of expression occurs in a wide variety of tumor cells. Applicants submit that the data provided establishes a reasonable relationship between expression of a nucleic acid encoding a polypeptide having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:6. A reasonable correlation between in vitro model to a disease state is all that is required to meet the enablement requirement.

Applicants also submit that the specification provides information sufficient to enable one of skill in the art to use the claimed method. A skilled artisan does not need specific instruction to determine the amount or presence or absence of the genus of nucleic acid molecules presented in claim 19. General methodology, including hybridization conditions are well known and available in common sources such as Methods of Enzymology and Molecular Cloning, A Laboratory Manual and have been described in the specification at page 17, line 7 to

page 18, line 7. In addition, it is well accepted that nucleic acid sequences having less than full identity may be detected through simple hybridization methods and nucleic acids probes for such detection are readily predicted and produced. Therefore, determining the amount or presence or absence of the genus of nucleic acid molecules is a matter of performing commonly employed laboratory techniques which do not require further explanation beyond that already provided in the specification.

Regarding polypeptides having at least 90% sequence identity with SEQ ID NO:6, structural information, as well as multiple comparisons to the human ortholog (SEQ ID NO:6) and S100 family members are provided in Figures 4B-4E. In these figures, identical or conserved amino acids residues are indicated in black shading (page 9, lines 12-16). The specification indicates that amino acids shaded in grey can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function. (Page 9, lines 17-19). The specification further directs that non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function. (Page 9, lines 19-20).

The above described comparisons, additionally supported by guidance on sequence identity on page 15, lines 8-18 and discussion of variants at pages 16-20 provides more than adequate guidance to one of skill in the art. Therefore, the claimed methods may readily be employed without undue experimentation. Examiner's assertion of an unreasonable number of inoperative polypeptides is unsupported in light of the evidence presented and the legal standard. Withdrawal of the enablement rejection is respectfully requested.

Based on the foregoing, Applicants request withdrawal of the rejection on this basis.

### **35 U.S.C. § 112, ¶1 Written Description**

Claim 19 was also rejected under 35 U.S.C. § 112, ¶1 because the Examiner, while indicating that the specification does reasonably provide written description for nucleic acids encoding SEQ ID NO: 6 and SEQ ID NO:3, contends that nucleic acid sequences encoding variants/mutations of SEQ ID NO:3 and SEQ ID NO:6 are not adequately supported. In particular, the rejection asserts that the skilled artisan cannot envision the detailed chemical



structure of the encompassed polypeptides and polynucleotides, and therefore conception is not achieved until reduction to practice has occurred. Applicants respectfully traverse.

The written description requirement is satisfied when Applicants' specification conveys with reasonable clarity to those skilled in the art, that as of the filing date sought, he or she was in possession of the invention. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). A written description of an invention involving a chemical genus requires a precise definition, such as by structure, formula ... of the claimed subject matter sufficient to distinguish it from other materials. Univ. of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1405 (Fed. Cir. 1997) (emphasis added). Since one skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass, such a formula is normally an adequate description of the claimed invention. Id. at 1406 (emphasis added). Moreover, as noted in the Guidelines for Examination of Patent Applications Under 35 U.S.C. § 112, ¶1, "Written Description" Requirement ("the guidelines"), there is a "strong presumption" that an adequate written description of the claimed invention is present when the application is filed, 66(4) Fed. Reg. 1099, 1105 (2001); see also, In re Wertheim, 191 USPQ 90,97 (CCPA 1976). The guidelines further state that "[The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims." 66(4) Fed. Reg. at 1107; 191 USPQ at 97, (emphasis added).

Claim 19 is directed to a method for determining the amount of a nucleic acid molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:3 or a polypeptide having at least 90% identity with the amino acid sequence of SEQ ID NO:6 in a sample.

In the specification, the sequence and thereby the complete chemical structure of the polypeptide of SEQ ID NOS:3 and 6 are provided. In addition, the relationship between the sequences, e.g, comparison between SEQ ID NO:3 and SEQ ID NO:6 is shown in Figure 2 and is described in the detailed description at page 9, lines 12-24. In Figure 2, the regions of identity are identified in the darkened blocks supporting the conclusion that the sequences are orthologs and provide further structural information regarding regions of amino acid conservation. Additional structural comparisons are made between SEQ ID NO:3 and its human ortholog SEQ ID NO:6 in Figures 4A through 4E, which illustrate the significant homology between SEQ ID

NO:3, SEQ ID NO:6 and other members of the S100 cytokine family. Figure 4A is a BLOCKS protein domain analysis of the polypeptide of SEQ ID NO:6 with other calcium binding proteins (SEQ ID NOs:12-36) which shows the two conserved calcium binding regions separated by 8 amino acids, which is characteristic of S100 proteins. (Page 9, lines 9-11). Figure 4B shows an alignment of the amino acids 28-131 of SEQ ID NO:3 with amino acids 1-101 of Acc. No. AY007220 (SEQ ID NO:39), an S100 type calcium binding protein and the resulting consensus sequence (SEQ ID NO:40). Figure 4D shows an alignment of calcium binding domains including amino acids 46 to 85 of SEQ ID NO:3 with various calcium binding proteins.

In these figures, identical or conserved amino acids residues are indicated in black shading. As directed by the specification, amino acids shaded in grey can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function. Non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function. (Page 9, lines 19-20.) Claim 19, as amended, provides a method for determining the amount of a nucleic acid encoding a polypeptide having at least 90% identity to the amino acid sequence of SEQ ID NO:6. The above described comparisons, additionally supported by guidance on sequence identity on page 15, lines 8-18 and discussion of variants at pages 16-20 provides more than adequate guidance to one of skill in the art to recognize the claimed invention from Applicant's disclosure and sufficient recitation of distinguishing identifying characteristics to define the envisioned polypeptides. In addition, nucleic acids encoding SEQ ID NO:3 and SEQ ID NO:6 are provided and may readily be employed to detect nucleic acids encoding the remaining polypeptides, such as is described at, for example, page 57, lines 17-30, as well as pages 20-22, and 55-60.

Therefore, Applicants respectfully request withdrawal of the rejection of the claims under the written description requirement.

### **35 U.S.C. § 112, ¶2 Indefiniteness**

On page 17 of the current Office Action, the Examiner rejected claims 19 and 38 under 35 U.S.C. § 112 ¶2 as indefinite for failing to set forth and distinctly claim the subject matter which Applicant regards as the invention. Applicants respectfully traverse.

The Examiner further points out that claim 38 fails to recite a polynucleotide sequence and therefore fails to set forth the metes and bounds of the invention claimed. While not acquiescing to the rejection, claims 19 and 38 now refer to a nucleic acid encoding a polypeptide having at least 90% sequence identity to the amino acid sequence of SEQ ID NO: 6 rendering the Examiner's rejection moot. Applicants respectfully request the withdrawal of this basis of rejection of claims 19 and 38.

Claims 19 and 38 are drawn to methods for determining the presence of a nucleic acid in a cell sample. The Examiner asserted that the methodology would require the use of hybridization conditions, which are missing from the claims, hence the claims fail to define the metes and bounds of the varying structures of polynucleotides recited in the claimed methods. The rejection continues, that stringency is relative and the specification does not provide an unambiguous definition for the term. Applicants respectfully disagree. Applicants assert that claims 19 and 38 do not lack definiteness due to lack of description of specific hybridization conditions.

The test for definiteness under 35 U.S.C. § 112, second paragraph, is whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification." *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576 (Fed. Cir. 1986). Furthermore, a claim term that is not used or defined in the specification is not indefinite if the meaning of the claim term is discernible. *Bancorp Services, L.L.C. v. Hartford Life Ins. Co.*, 359 F.3d 1367, 1372 (Fed Cir. 2004). MPEP 2173.02.

Applicants submit that methods of determining the presence or amount of a nucleic acid in a sample are well known in the art. In addition, Applicants have described such detection methods at pages 17-19 in the specification. Design of probes, length of probes and T<sub>m</sub> of probe to the target sequence can readily be determined by one of skill in the art having the nucleic acid sequence. Applicants have also described and provided specific examples of probes and/or primers at page 86.

Thus, Applicants submit the claims are not indefinite and respectfully request withdrawal of the rejection.

**Interview**

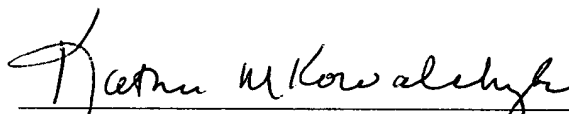
Applicants request an interview with the Examiner and her supervisor upon receipt of these papers.

**Summary**

Applicants respectfully request entry of the above amendments. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,  
MERCHANT & GOULD P.C.  
P.O. Box 2903  
Minneapolis, Minnesota 55402-0903  
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Date: November 13, 2006



Katherine M. Kowalchyk  
Reg. No. 36,848  
KMK/LPS:sab



Figure 1.



Sequence type explicitly set to Protein  
Sequence format is Pearson  
Sequence 1: new\_S100\_cytokine 104 aa  
Sequence 2: G491246 110 aa  
Sequence 3: W27152 98 aa

Start of Pairwise alignments

Aligning...

Sequences (1:2) Aligned. Score: 23

Sequences (1:3) Aligned. Score: 34

Sequences (2:3) Aligned. Score: 29

Start of Multiple Alignment

There are 2 groups

Aligning...

Group 1: Delayed

Group 2: Delayed

Sequence:1 Score:0

Sequence:3 Score:839

Sequence:2 Score:724

Alignment Score 444

CLUSTAL-Alignment file created [/data4/genetools/lrastelli4630clustalw]

Image replaced with  
identical better quality  
image and repositioned.

#### Multiple Alignment:

```
new_S100_cytokine  MQQCRSANAED...QEF...ETIKNFHOYSWEG...STLTPSE...RNTQOLPHIMP
W27152             .....MAEPI...ES...ET...TFFTEARQER...SVNE...ELVTQOLPHLP
G491246            .....MQQ...ETIKNFHOYSWKL...PDTLNQ...ELRKOLQNF...

new_S100_cytokine  SNCG...LEENYAN...SCND...KERS...WELIGEA...SVKLE...VREH... (SEQ ID NO:6)
W27152             DVOS...LDEHK...SVN...SELK...NEY...RLIGELA...EIRK...L...LIRKK... (SEQ ID NO:10)
G491246            KENKNEKV...EH...MED...L...AD...K...S...E...I...M...AR...TWASHE...MHEGDEGP...E...H...K...P...L...G

new_S100_cytokine  .... (15-119 of SEQ ID NO:6)
W27152             .... (SEQ ID NO:10)
G491246            EGTG (SEQ ID NO:11)
```

Figure 4B

Table 3  
AY007220  
Consensus

10	20	30	40	50	60
MGQCRSANAEDAQEFSDVERAIETLIK	NFFNTSVASKKETLTLP	ELRDLVTQQLPHLMPS			
MGQCRSANAEDAQEFSDVERAIETLIK	NFFNTSVASKKETLTLP	ELRDLVTQQLPHLMPS			
MGQCRSANAEDAQEFSDVERAIETLIK	NFFNTSVASKKETLTLP	ELRDLVTQQLPHLMPS			

Table 3  
AY007220  
Consensus

70	80	90	100
NCGLEEKIANLG	CNDSKLEF	CSFWELIGEAAKSVK	ERP
NCGLEEKIANLG	CNDSKLEF	CSFWELIGEAAKSVK	ERP
NCGLEEKIANLG	CNDSKLEF	CSFWELIGEAAKSVK	ERP

(SEQ ID NO:3)  
(SEQ ID NO:39)  
(SEQ ID NO:40)

Delete  
Figure is a  
duplicate.

Figure 4A.

# BLOCKS Protein Domain Analysis of new\_S100\_cytokine

Probe Size: 104 Amino Acids

Probe File: lrastelliblocks.seq

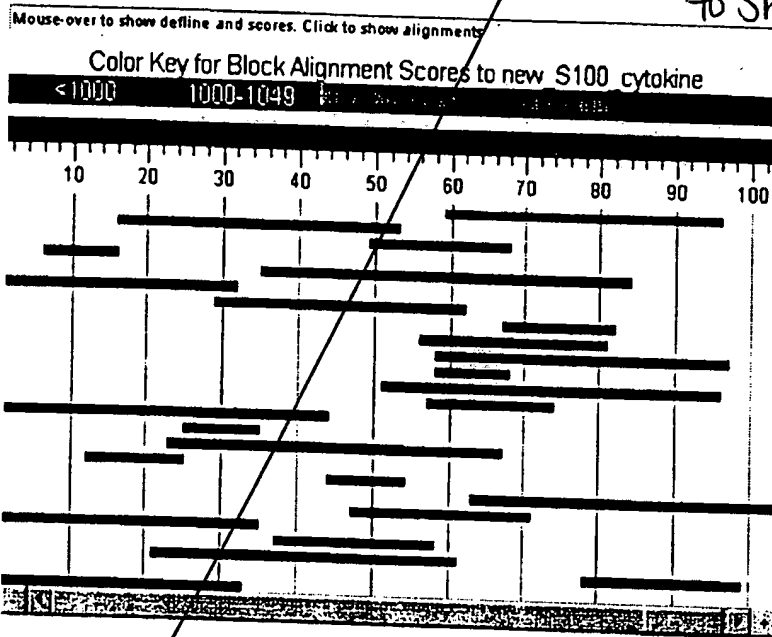
Target File (s) : blocks.dat

Records Searched: 4034

Scores Done: 4034

Alignments Done: 535470

Enlarged  
Moved  
to Sheet 4



Enlarged  
and  
rotated

Accession	Description	Strength	Score	EF	Accession	Description
EL000012	1-100/IL12 type calcium binding protein.	1335	1057	0	59	AKG12211 (SEQ ID NO:12)
EL00002A	1-100/IL12 type calcium binding protein.	1345	1070	0	16	DV041211 (SEQ ID NO:13)
EL00004A	Bacterial type II secretion system protein F	1456	1021	0	49	VT001411 (SEQ ID NO:14)
EL00007B	Ubiquitin carboxyl-terminal hydrolase family	1227	992	0	5	5A01007 (SEQ ID NO:15)
EL00008C	Bacterial chemotaxis sensory transducer protein	1750	990	0	35	GA001171 (SEQ ID NO:16)
EL00009D	Phosphoenolpyruvate carboxylase (ATP) protein	1412	989	0	9	0401010 (SEQ ID NO:17)
EL00010A	Prokaryotic-type carboxyl anhydrase proteins	1539	981	0	29	0401010 (SEQ ID NO:18)
EL00011E	Ergosterol biosynthesis ERG4/ERG16 family protein	1499	981	0	67	1001010 (SEQ ID NO:19)
EL00012E	Lysosome-associated membrane glycoprotein 2	1533	976	0	56	1001010 (SEQ ID NO:20)
EL00013E	Phosphotransferase protein	1501	976	0	58	1001010 (SEQ ID NO:21)
EL00014E	PB domain protein profile	990	976	0	58	1001010 (SEQ ID NO:22)
EL00015E	Myosin protein	1173	976	0	61	1001010 (SEQ ID NO:23)
EL00016E	Phosphatidylserine-specific phospholipase X	1403	976	0	57	1001010 (SEQ ID NO:24)
EL00017E	Glycine protein	1500	972	0	1	1001010 (SEQ ID NO:25)
EL00018E	Membrane attack complex component / perforin	1127	971	0	21	1001010 (SEQ ID NO:26)
EL00019E	Drosophila melanogaster protein	1592	970	0	23	1001010 (SEQ ID NO:27)
EL00020E	Phosphoglycerate mutase family phosphatidyl	1290	960	0	1	1001010 (SEQ ID NO:28)
EL00021E	Ribosomal protein L12 protein	1092	967	0	44	1001010 (SEQ ID NO:29)
EL00022E	1'-5'-oligoadenylate synthetase protein	1026	967	0	53	1001010 (SEQ ID NO:30)
EL00023E	Formate and nitrite transporters protein	1561	964	0	47	1001010 (SEQ ID NO:31)
EL00024E	Glycoprotein homodimer: beta chain protein	1520	963	0	1	1001010 (SEQ ID NO:32)
EL00025E	Vinculin family talin-binding region protein	1507	963	0	37	1001010 (SEQ ID NO:33)
EL00026E	Beta-lactamase class B protein	1500	960	0	21	1001010 (SEQ ID NO:34)
EL00027E	Heat shock hsp60 protein family profile	1100	960	0	70	1001010 (SEQ ID NO:35)
EL00028E	Hydroxymethylglutaryl-coenzyme A lyase protein	1500	960	0	1	1001010 (SEQ ID NO:36)

Figure 4B.

Table3  
AA007220 AY007220  
Consensus

```

      10      20      30      40      50      60
.....|.....|.....|.....|.....|.....|
MGQCRSANAEDAQEFSDVERAIETLIKNFHYSVAASKKETLTPSELRLDVTQQLPHLMPS
MGQCRSANAEDAQEFSDVERAIETLIKNFHYSVAASKKETLTPSELRLDVTQQLPHLMPS
MGQCRSANAEDAQEFSDVERAIETLIKNFHYSVAASKKETLTPSELRLDVTQQLPHLMPS

```

Table3  
AA007220  
Consensus

```

      70      80      90     100
.....|.....|.....|.....|
NCGLEEKIANLGNCDNSKLEFRSFWELIGEAAKSVKLERPV (SEQ ID NO:3)
NCGLEEKIANLGNCDNSKLEFRSFWELIGEAAKSVKLERPV (SEQ ID NO:39) (1-101)
NCGLEEKIANLGNCDNSKLEFRSFWELIGEAAKSVKLERPV (SEQ ID NO:40)

```

amino acids 28-128 of

Figure 4C.

Table 6  
AA007220  
Consensus

```

      10      20      30      40      50      60
.....|.....|.....|.....|.....|.....|
MGQCRSANAEDAQEFSDVERAIETLIKNFHQYSVEGGKETLTPSELRLDVTQQLPHLMPS
MGQCRSANAEDAQEFSDVERAIETLIKNFHQYSVEGGKETLTPSELRLDVTQQLPHLMPS
MGQCRSANAEDAQEFSDVERAIETLIKNFHQYSVEGGKETLTPSELRLDVTQQLPHLMPS

```

Table 6  
AA007220  
Consensus

```

      70      80      90     100
.....|.....|.....|.....|
NCGLEEKIANLGNCDNSKLEFRSFWELIGEAAKSVKLERPVGRH (SEQ ID NO:6)
NCGLEEKIANLGNCDNSKLEFRSFWELIGEAAKSVKLERPVGRH (SEQ ID NO:39)
NCGLEEKIANLGNCDNSKLEFRSFWELIGEAAKSVKLERPVGRH (SEQ ID NO:40)

```

amino acids 15-118 of

Figure 4D.

Table 3  
gi|4139958|pdb|1MHO|  
PROTEIN MRP-126  
ICTACALCIN  
CALGRANULIN B  
Consensus

```

      10      20      30      40
.....|.....|.....|.....|
EKATITLIKNFHYSVAASKKETLTPSELRLDVTQQLPHLMPS (SEQ ID NO:3)
EKATITLIKNFHYSVAASKKETLTPSELRLDVTQQLPHLMPS (SEQ ID NO:41)
EKATITLIKNFHYSVAASKKETLTPSELRLDVTQQLPHLMPS (SEQ ID NO:42)
EKATITLIKNFHYSVAASKKETLTPSELRLDVTQQLPHLMPS (SEQ ID NO:43)
EKATITLIKNFHYSVAASKKETLTPSELRLDVTQQLPHLMPS (SEQ ID NO:44)
EKATITLIKNFHYSVAASKKETLTPSELRLDVTQQLPHLMPS (SEQ ID NO:45)

```

amino acids 46-85

Figure 4E.

Table 6  
gi|4139958|pdb|1MHO|  
PROTEIN MRP-126  
CALGRANULIN B  
CALGRANULIN B  
Consensus

```

      10      20      30      40
.....|.....|.....|.....|
EKATITLIKNFHYSVAASKKETLTPSELRLDVTQQLPHLMPS (SEQ ID NO:6)
EKATITLIKNFHYSVAASKKETLTPSELRLDVTQQLPHLMPS (SEQ ID NO:41)
EKATITLIKNFHYSVAASKKETLTPSELRLDVTQQLPHLMPS (SEQ ID NO:42)
EKATITLIKNFHYSVAASKKETLTPSELRLDVTQQLPHLMPS (SEQ ID NO:44)
EKATITLIKNFHYSVAASKKETLTPSELRLDVTQQLPHLMPS (SEQ ID NO:46)
EKATITLIKNFHYSVAASKKETLTPSELRLDVTQQLPHLMPS (SEQ ID NO:47)

```

amino acids 33-72



Figure 7

(Table changed From portrait to landscape orientation)

***** Contig 1 *****	
65677221+	GAATTCCAGAGGGAGTTCTCAGTGCCCCCGGACAGGCCTCTCCAGCTTCACACTCTTGGC
AA315020-	TGCCCCCGGACAGTCCTCTCNAGCTTCACACTCTTGGC
<b>consensus</b>	GAATTCCAGAGGGAGTTCTCAGTGCCCCCGGACAGGCCTCTCCAGCTTCACACTCTTGGC
65677221+	CGCTTCTCCAATCAGCTCCCAGAACTCCTGAACTCCAGTTTAGAGTCATTGCAGCTGCC
AA315020-	CGCTTCTCCAATCAGCTCCCAGAACTCCTGAACTCCAGTTTAGAGTCATTGCAGCTGCC
<b>consensus</b>	CGCTTCTCCAATCAGCTCCCAGAACTCCTGAACTCCAGTTTAGAGTCATTGCAGCTGCC
65677221+	CAGGTTGGCAATTTTCTCTTCCAGGCCACAGTTGCTCGGCATGAGATGGGGCAGCTGCTG
AA315020-	CAGGTTGGCAATTTTCTCTTCCAGGCCANAGTTGCTCGGCATGAGATGGGGCAGCTGCTG
<b>consensus</b>	CAGGTTGGCAATTTTCTCTTCCAGGCCACAGTTGCTCGGCATGAGATGGGGCAGCTGCTG
65677221+	GGTGACCAGGTCCCGTAGCTCAGAAGGGGTCAGCGTCTCCTTCCCACCCTCCACGGAGTA
AA315020-	GGTGACCAGGTCCCGTAGCTCAGAAGGGGTCAGCGTCTCCTTCCCACCCTCCACGGAGTA
<b>consensus</b>	GGTGACCAGGTCCCGTAGCTCAGAAGGGGTCAGCGTCTCCTTCCCACCCTCCACGGAGTA
65677221+	CTGGTGAAAGTTCTTGATGAGGGTCTCAATGGCCCTCTCCACATCACTGAATTC (SEQ ID NO:37)
AA315020-	CTGGTGAAAGTTCTTGATGAGGGTCTCAATGGCCCTCTCCACATCACTGAATTCCTGAGC
<b>consensus</b>	CTGGTGAAAGTTCTTGATGAGGGTCTCAATGGCCCTCTCCACATCACTGAATTCCTGAGC
AA315020-	ATCCTCTGCGTTGGCTGACCGACACTGTCCCATGGTGCTCACTGTGTCTGGTCCTTTGGT
<b>consensus</b>	ATCCTCTGCGTTGGCTGACCGACACTGTCCCATGGTGCTCACTGTGTCTGGTCCTTTGGT
AA315020-	GAGAGTTCTGTTGTCCTAT (SEQ ID NO:47-48)
<b>consensus</b>	GAGAGTTCTGTTGTCCTAT (SEQ ID NO:5)